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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/082,112	05/20/1998	ALBERTO L. MENDOZA	MSU4.1-406	2322

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/082,112	MENDOZA, ALBERTO L.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

Applicant's amendment filed 3/20/2006 is acknowledged. Claim 25 has been cancelled. Claims 16 and 18 have been amended. Claims 16-24 are pending and currently under examination.

Specification Objection Maintained

The amendment filed 10/8/1999 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendment changes the strain of *Pythium insidiosum* from ATCC strain 58643 to ATCC strain 74446. This is deemed new matter lacking specific written description support in the specification as filed.

Applicant argues that the organism known as ATCC strain 58643 is identical to ATCC strain 74446, thus an amendment to the specification changing the deposited strain number is not new matter. Applicant has asserted that an ATCC Budapest Treaty Receipt and Viability statement for ATCC designation 74446 has been submitted to the office as evidence that said strains are identical.

Applicant's arguments have been fully considered and deemed non-persuasive. No ATCC Budapest Treaty Receipt and Viability statement for ATCC designation 74446 has been received, and no explanation has been presented regarding the reason for a redeposit of strain 58643. Replacement deposits are not recognized by the office where the depository could furnish samples of the deposit being replaced (MPEP 1.805).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections Withdrawn

The rejection of claims 16-18 and 20-22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn. Applicant's amendments to claims 16 and 18 render this rejection moot.

The rejection of claim18 and dependent claims 20-22 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in light of applicant's amendment to claim 18.

The rejection of claim 25 under 35 U.S.C. 103(a) as being unpatentable over Mendoza *et al.* (92a)(Mycopathologia 119:89-95, 1992), Mendoza *et al.* (92b)(J. Clinical Microbiol, 30:2980-2983, 1992), Mendoza (3rd NIAID Workshop in Med. Mycol. Series Abstracts, 1995), Amicon 1993 catalog, and Fisher 1995 catalog as applied to claims 18, 20-22 above, and further in view of Blanch *et al.* (Biochemical Engineering, Marcel Dekker, Inc., 1996), is withdrawn. The cancellation of claim 25 renders this rejection moot.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the office action filed 12/21/2005. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claim as originally filed recites *Pythium insidiosum* ATCC strain 58643, whereas the amendment filed 10/8/1999 changes the strain to ATCC strain 74446. This is deemed new matter lacking specific written description support in the specification as filed.

Applicant argues that the organism known as ATCC strain 58643 is identical to ATCC strain 74446, thus an amendment to the specification changing the deposited strain number is not new matter. Applicant has asserted that an ATCC Budapest Treaty Receipt and Viability

statement for ATCC designation 74446 has been submitted to the office as evidence that said strains are identical.

Applicant's arguments have been fully considered and deemed non-persuasive. No ATCC Budapest Treaty Receipt and Viability statement for ATCC designation 74446 has been received, and no explanation has been presented regarding the reason for a redeposit of strain 58643. Replacement deposits are not recognized by the office where the depository could furnish samples of the deposit being replaced (MPEP 1.805).

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18, 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendoza *et al.* (92a)(Mycopathologia 119:89-95, 1992) in view of Mendoza *et al.* (92b)(J. Clinical Microbiol, 30:2980-2983, 1992), Mendoza (3rd NIAID Workshop in Med. Mycol. Series Abstracts, 1995), Amicon 1993 catalog, and Fisher 1995 catalog for the reasons set forth in the office action filed 12/21/2005.

The instant claims are drawn to a method for treatment of an infection caused by *Pythium insidiosum* in a mammal which comprises providing an injectable vaccine comprising:

1. mixed intracellular proteins, which consist essentially of proteins removed from disrupted cells of *Pythium insidiosum* separated from the culture medium; and
2. mixed extracellular proteins, which consist essentially of proteins removed from the culture medium separated from the cells of the *Pythium insidiosum*;

wherein the admixture of proteins has been precipitated from the culture medium with acetone and admixed with water and then has been dialyzed to remove low molecular weight components less than 10,000 MW (claim 18). Further limitations include the method of claim 18 where the cells have been disrupted by sonication (claim 20), where the *Pythium insidiosum* is deposited as

ATCC 74446 (claim 21), and where the culture medium is Sabouraud's dextrose broth (claim 22).

Applicant argues:

1. That the vaccines disclosed in the prior art were of limited value for treating horses infected greater than 0.5 months but less than 2 months, and neither vaccine was effective for treating horses that had been infected for more than 2 months. Applicant also states that the art shows that immunotherapy has several drawbacks, including the development of severe inflammatory reactions at the vaccination site. Applicant states that the presence of a property not possessed by the prior art is evidence of nonobviousness and that the absence of a property which a claimed invention would have been expected to possess is evidence of unobviousness. Applicant argues that the claimed vaccine has remarkably enhanced curative properties over the vaccines of the prior art, and that the claimed vaccine causes only mild inflammatory reactions, whereas the vaccines of the prior art caused severe reactions and abscesses at the site of injection. Applicant states that a cure-rate of 50% of cases older than 2 months was achieved and that this property is lacking in the prior art.

2. That Mendoza (92b) suggests the use of immunodominant proteins in immunotherapy, but does not disclose a vaccine.

3. That the combination of references does not show or suggest the use of a vaccine containing mixed intracellular proteins and mixed extracellular proteins that is prepared so as to only lead to a mild inflammatory response when injected. Applicant argues that it would be unexpected that such a vaccine would not cause a more severe inflammation at the injection site, based on the teachings of the prior art. Applicant further argues that, while the art suggests adding the immunodominant intracellular proteins to the extracellular proteins, the art does not suggest that the improved results would not have the inflammation associated with the vaccines of the prior art.

4. That the Amicon catalog, in combination with the other references does not suggest that the use of a PM10 membrane would improve the inflammation problem associated with prior vaccines.

5. That Mendoza (92b) teaches the use of a PM10 membrane to concentrate the extracellular proteins of *Conidiobolus coronatus*, and not the intracellular proteins of *Pythium insidiosum*.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, the duration of the horse's infection is not a limitation that is in the claims. Further, the combination of the cited references would result in a composition that is identical to the claimed vaccine. The term "vaccine" is an intended use and is given no patentable weight. Said composition would have the same physical, chemical, and immunological properties as the claimed vaccine. There has been no showing that the claimed vaccine is different than the combination of the prior art. Since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Applicant's statement that the claimed vaccine has remarkably enhanced curative properties and mild reactions is unsubstantiated. The declaration under 37 CFR 1.132 by the inventor does not show data from a comparison of the claimed vaccine with those of the prior art. What little data applicant shows is not a comparison between the vaccines of the prior art and the claimed vaccine, and of the data shown, applicant even reports that there were no data available for one third of the animals used in their studies. Further, Mendoza (92a) stated that the inflammatory response was a function of the amount of vaccine inoculated. The authors were able to obtain a suitable response without severe inflammatory reactions using both types of vaccines (see page 92, column 2, paragraph 3). With no data to compare the claimed vaccine and the vaccines of the prior art, and with the suggestion of Mendoza (92a), the skilled artisan would believe that the lack of inflammatory reaction in the claimed vaccine resulted from the optimization of the amount of antigen delivered, rather than some unexpected property. With regard to the remarkable curative properties of the claimed vaccine, applicant's declaration states that a cure-rate of 50% of cases older than 2 months was achieved and that this property is lacking in the prior art. Mendoza (96) disclosed that a modification of previous vaccines led to an increase in the number of cured cases, and that 50% of horses with chronic pythiosis (>2 months) responded to this modified

vaccine, and that the horses that had not previously responded did not develop swellings at the vaccination site (see page 161, paragraph bridging columns 1-2).

Regarding argument 2, it is the combination of references which renders the instantly claimed invention obvious, not the disclosure of Mendoza (92b) alone. However, contrary to applicant's assertion, Mendoza (92b) specifically suggests the use of the three immunodominant antigens as vaccines (see page 2982, column 2, paragraph 3). Moreover, the term "vaccine" is an intended use and is given no patentable weight. The compositions suggested for use in immunotherapy by the combination of prior art references is identical to the claimed composition intended for use in immunotherapy.

Regarding argument 3, it is noted that the features upon which applicant relies (i.e., a vaccine containing mixed intracellular proteins and mixed extracellular proteins that is prepared so as to only lead to a mild inflammatory response when injected) are not recited in the rejected claims. Applicant has claimed a method of treatment using a vaccine that contains mixed intracellular proteins and mixed extracellular proteins. As stated above, the combination of the cited references would result in a composition that is identical to the claimed vaccine, and which would have the same physical, chemical, and immunological properties as the claimed vaccine. Further, as stated above, Mendoza (92a) stated that the inflammatory response was a function of the amount of vaccine inoculated, and a mere optimization of these amounts led to elimination of said inflammatory reaction.

Regarding argument 4, as stated above, optimization of the antigen dose, as disclosed by Mendoza (92a) improves the inflammation problem associated with prior vaccines.

Regarding argument 5, the claim is drawn to a method of treatment using a vaccine that contains mixed intracellular proteins and mixed extracellular proteins, produced by a specific method. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Regardless of whether one uses a PM10 membrane or dialysis tubing, the claimed vaccine, and those of the prior art have been rid of molecules that are less than 10,000 molecular weight.

As outlined previously, Mendoza *et al.* (92a) teach subcutaneous administration of two vaccines for pythiosis, the Cell Mass Vaccine (CMV), and the Soluble Concentrated Antigen Vaccine (SCAV) to mammals. The CMV consists of mixed intracellular antigens of *P. insidiosum* obtained by culturing *P. insidiosum* (ATCC 58643) in Sabouraud's dextrose broth. The cells were removed from the culture medium and disrupted by homogenization to provide the antigens for the vaccine (p. 90, col. 2). The SCAV consists of extracellular proteins obtained by culturing *P. insidiosum* (ATCC 58643) in Sabouraud's dextrose broth. The extracellular antigens were concentrated with a stir cell and precipitated with acetone (p. 91, col. 2 and p.92 col. 1). Mendoza *et al.* (92a) teach that both vaccines were successful in curing cases of pythiosis in horses (p. 91, col. 2, paragraph 2). Mendoza *et al.* (92a) further teaches that the etiological agent of pythiosis in horses, cattle, dogs, cats, and humans is *Pythium isidiosum*, and that nine strains isolated from humans, horses, and dogs with the disease were all the same species (p. 89, paragraph 1). Mendoza *et al.* (92a) does not teach that the intracellular proteins are separated from the disrupted cells in the CMV or the use of sonication to disrupt the cells. Mendoza *et al.* (92a) further does not teach the use of dialysis to remove components less than 10,000 MW or a vaccine that is a mixture of the intracellular and extracellular proteins.

Mendoza *et al.* (92b) teach alternative methods to produce intracellular and extracellular protein pythiosis vaccines. The vaccine containing the intracellular proteins was produced by culturing *P. insidiosum*, killing the cells with Methiolate (thimersol), sonicating the cells to disrupt them and release intracellular proteins, then separated from the cell debris by centrifugation (p. 2981, col. 1, paragraph 1). An alternative method to produce a vaccine containing extracellular proteins is also taught. Cultures were killed with Merthiolate (thimersol), filtered to remove cells, and a stir cell with PM-10 membrane (Amicon) was used to concentrate the antigen (and remove low molecular weight components)(p. 2981, col. 1, paragraph 2). They also teach the important antigens found in the CMV vaccine and disclose that in addition to three immunodominant proteins (32K, 30K, and 28K) there are at least 20 antigens found in the intracellular proteins of *Pythium isidiosum* that are reactive in horse sera (p. 2981, col. 2, paragraph 3) and suggest that vaccines should include the three immunodominant proteins (p. 2982, col. 2, paragraph 3). Mendoza *et al.* (92b) also teach that five strains of *Pythium isidiosum* all had similar intracellular protein profiles.

Mendoza (95) teaches a vaccine that combined extracellular pythium antigens and the three immunodominant intracellular proteins of Mendoza (92b) and that said vaccine had an enhanced therapeutic effect on horses (see abstract). Mendoza (95) further teaches that hyphal antigens may contain products that are directly involved in the enhancement of the immunological response to vaccination (see abstract).

The Amicon 1993 catalog teaches that a PM10 membrane will retain molecules larger than 10,000 MW (p. 35).

The Fisher 1995 catalog teaches dialysis membranes which will retain molecules larger than 10,000 MW (p. 56).

As to claims 18, 20-22, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to administer, to mammals, a pythiosis vaccine comprising a mixture of mixed intracellular proteins (especially including the three immunodominant proteins of Mendoza (92b)) and mixed extracellular proteins because Mendoza (95) teaches that a vaccine comprising a mixture of three immunodominant intracellular proteins and extracellular proteins was more successful in curing horses than either the CMV or SCAV vaccines, and because Mendoza (92b) teaches that there are at least 20 reactive antigens found in the intracellular proteins of *Pythium isidiosum* that might be useful in immunotherapy. It would also have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to use the method obtain the intracellular antigens by culturing *P. insidiosum*, killing the cells with Methiolate (thimersol), sonicating the cells to disrupt them and release intracellular proteins, then separated from the cell debris by centrifugation because it would be easier to obtain the intracellular proteins this way, than using electrophoresis to obtain only the three immunodominant proteins. The ordinary artisan would also have been motivated to use dialysis instead of a stir-cell with a PM10 membrane because dialysis is significantly cheaper and provides for large batches. Further, as taught by the Amicon and Fisher catalogs, the removal of small molecules of less than 10,000 MW by the PM10 membrane and the dialysis membrane is functionally equivalent.

Consequently, the rejection is deemed proper and is maintained.

Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendoza *et al.* (92a)(Mycopathologia 119:89-95, 1992), Mendoza *et al.* (92b)(J. Clinical Microbiol, 30:2980-2983, 1992), Mendoza (3rd NIAID Workshop in Med. Mycol. Series Abstracts, 1995), Amicon 1993 catalog, and Fisher 1995 catalog as applied to claims 18, 20-22 above, and further in view of Mendoza *et al.* (J. Mycol. Med., 6:151-164, 1996) for the reasons set forth in the office action filed 12/21/2005.

The instant claims are drawn to a method for treatment of an infection caused by *Pythium insidiosum* in humans which comprises providing an injectable vaccine comprising:

1. mixed intracellular proteins, which consist essentially of proteins removed from disrupted cells of *Pythium insidiosum* separated from the culture medium; and
2. mixed extracellular proteins, which consist essentially of proteins removed from the culture medium separated from the cells of the *Pythium insidiosum*;

wherein the admixture of proteins has been precipitated from the culture medium with acetone and admixed with water and then has been dialyzed to remove low molecular weight components less than 10,000 MW (claim 16), and wherein said vaccination is subcutaneous (claim 17).

Applicant argues:

1. That the combination of references does not suggest that the vaccine prepared in the claimed method would improve the inflammation problem associated with the vaccines of the prior art, and that it would not be obvious that such a vaccine would be safe enough for the treatment of humans.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, as stated above, optimization of the antigen dose, as disclosed by Mendoza (92a) improves the inflammation problem associated with prior vaccines. Further, the combination of the cited references would result in a composition that is identical to the claimed vaccine. Said composition would have the same physical, chemical, and immunological properties as the claimed vaccine. Since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See In

re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). There has been no showing that the claimed vaccine is different than the combination of the prior art.

As outlined previously, Mendoza *et al.* (92a), Mendoza *et al.* (92b), Mendoza (95), Amicon 1993 catalog, and Fisher 1995 catalog as combined over claims 18, 20-22 is set forth *supra*. The combination as set forth *supra* does not teach the treatment of pythiosis in humans using the vaccine as set forth above.

Mendoza *et al.* (96) teach the prevalence of human pythiosis and the need for an effective treatment for humans (p. 156, col. 2 and p. 160, col. 2, paragraph 2). They also teach the benefits of vaccination using intracellular (CMV) and extracellular (SCAV) antigens from *P. insidiosum* (p. 161, Immunotherapy). Mendoza *et al.* (96) further teach similarities in *P. insidiosum* antigens detected in human and horse sera (p. 159, Immunodiffusion test).

As to claims 16-17, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to use the mixed intra and extracellular vaccine combination set forth *supra* to treat humans because of the similarity in immune response in humans to that found in horses, because of the increased benefit seen by the combination in horses, and by the need for an effective treatment in humans.

Consequently, the rejection is deemed proper and is maintained.

Claims 19, 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendoza *et al.* (92a)(Mycopathologia 119:89-95, 1992), Mendoza *et al.* (92b)(J. Clinical Microbiol, 30:2980-2983, 1992), Mendoza (3rd NIAID Workshop in Med. Mycol. Series Abstracts, 1995), Amicon 1993 catalog, and Fisher 1995 catalog as applied to claims 18, 20-22 above, and further in view of Blanch *et al.* (Biochemical Engineering, Marcel Dekker, Inc., 1996) for the reasons set forth in the office action filed 12/21/2005.

The instant claims are drawn to a method for the treatment of Pythiosis in a mammal which comprises injecting a vaccine comprising:

1. mixed intracellular proteins, which consist essentially of proteins removed from disrupted cells of *Pythium insidiosum* separated from the culture medium; and
2. mixed extracellular proteins, which consist essentially of proteins removed from the culture medium separated from the cells of the *Pythium insidiosum*;

wherein the admixture of proteins has been precipitated from the culture medium with acetone and admixed with water and then has been dialyzed to remove low molecular weight components less than 10,000 MW (claim 19); wherein the culture medium is Sabouraud's dextrose broth (claim 22); wherein the cells have been killed with thimersol (claim 23); and wherein the disrupted cells are removed from the sterile water containing the mixed intracellular proteins by centrifugation to provide the mixed intracellular proteins of (1) in the second supernatant (claim 24).

Applicant argues:

1. That the combination of references does not suggest that the vaccine prepared in the claimed method would improve the inflammation problem associated with the vaccines of the prior art.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, as stated above, optimization of the antigen dose, as disclosed by Mendoza (92a) improves the inflammation problem associated with prior vaccines. Further, the combination of the cited references would result in a composition that is identical to the claimed vaccine. Said composition would have the same physical, chemical, and immunological properties as the claimed vaccine. Since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). There has been no showing that the claimed vaccine is different than the combination of the prior art.

As outlined previously, Mendoza *et al.* (92a), Mendoza *et al.* (92b), Mendoza (95), Amicon 1993 catalog, and Fisher 1995 catalog as combined over claims 18, 20-22 is set forth *supra*. The combination as set forth *supra* does not teach the use of acetone to precipitate proteins after the intracellular proteins have been mixed with the extracellular proteins.

Blanch *et al.* teach that one of the most common methods of precipitating proteins is through the addition of acetone, and that it is usually preferred over longer-chain organics (p. 491, paragraph 4 and p. 496, paragraph 2).

As to claims 19, 22-25, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to use acetone to precipitate the proteins of the invention because it is standard in the art to use acetone precipitation and because Blanch *et al.* teach that one of the most common methods of precipitating proteins is through the addition of acetone.

Consequently, the rejection is deemed proper and is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian Gangle
6/5/2006

ROBERT ZEMAN
PATENT EXAMINER